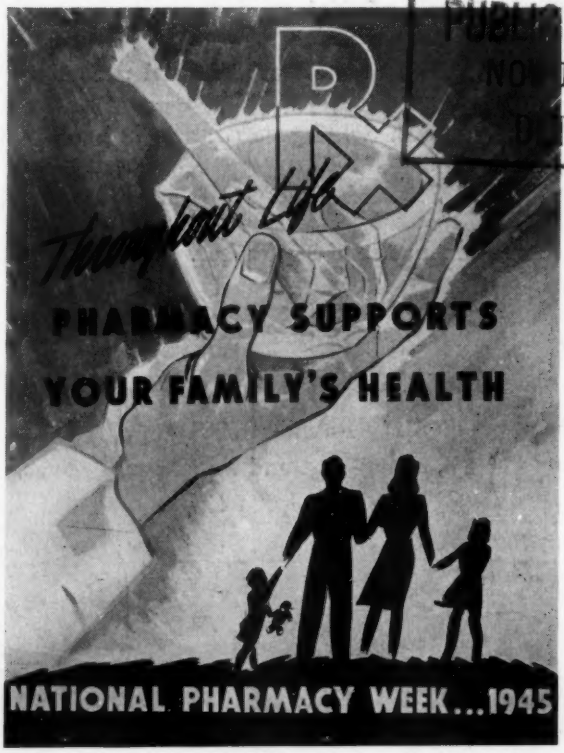
American Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH



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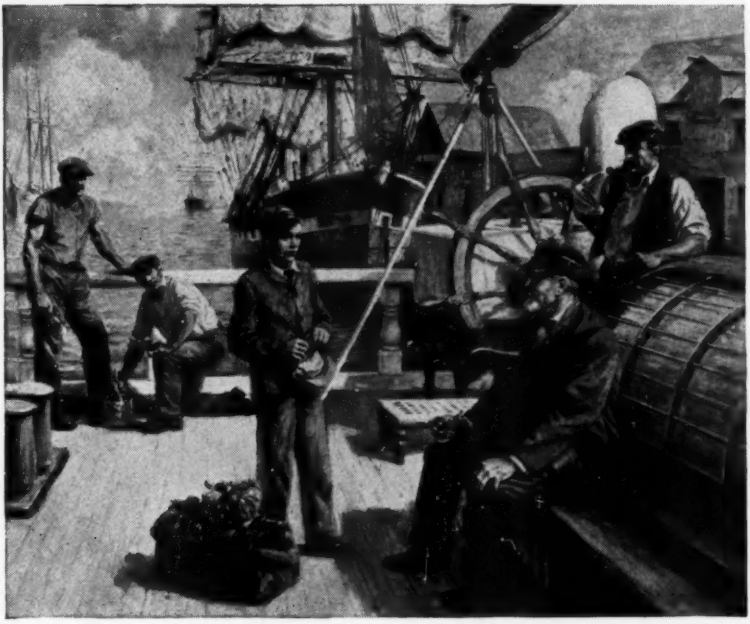

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Analgesic Calamine
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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

Vol. 117. AUGUST, 1945 No. 8

CONTENTS

OUR COVER

NATIONAL PHARMACY WEEK

THE annual observance of National Pharmacy Week imposes a responsibility upon each individual who considers himself or herself a member of the profession. Everyone can render some service in molding public opinion into a proper recognition of the services and importance of pharmacy in our national life and in the over-all picture of public health.

In deciding upon the type of public contact that may be best, each individual should consider those opportunities most likely to produce beneficial results with his particular training and experience. Thus college professors can stimulate their students to become emissaries of pharmacy's message and themselves appear before service clubs or other groups to discuss the many features of pharmacy which go unnoticed and unappreciated by too many people.

Commercial institutions should by well-conceived advertisements in popular magazines seek to carry the message to the great bulk of our population.

Retail pharmacists have the unique opportunity of doing the most important part. It is here that public opinion concerning pharmacy is most profoundly affected. Every pharmacist should try this week, with even more than customary effort, to convey to his customers and others the realization of the many valuable services which he as a pharmacist renders the community and that he is indeed in a higher category than a merchant. Let us not forget that people rarely evaluate a man above his own honest appraisal of his abilities. We must not only look and act the part but strive to be it also.

EDITORIAL

THE CONTROL OF BARBITURATES

A GREAT deal of agitation is prevalent for a more rigid control of the barbiturates, and legislation has been proposed in certain states placing these drugs in almost the same category as those controlled under the Harrison Act. The proponents of these measures claim that great damage is being done by the promiscuous sale and use of barbiturates and a number of these purported excesses are cited as examples. As usual it is the "unscrupulous" and "unethical" druggists who are played up in newspaper articles as largely responsible for this damage to society and public health. It would be well, however, to consider certain aspects of the problem which are relevant and not broadly defame pharmacists as the source of the entire evil.

Insomnia as a condition is more widely prevalent as time goes on and it will continue to be. This is part of the price which we pay for the intense mental activity so necessary in our highly developed civilization. As physical work becomes less and less a part of man's activity and mental and emotional stress takes its place, nerve strain and sleeplessness will continue to assume greater proportions as a medical problem. Man, the animal, was never intended by nature to assume the nerve-breaking mental tasks which are a part of millions' daily routine. It is all very well and good for someone to say that Mr. Jones should give up the position which exacts such a toll but unfortunately this is not always possible, let alone feasible. Another factor concerned is that a more phlegmatic individual than Mr. Jones would probably not even be able to perform the mental tasks which are a part of Mr. Jones' work and upon this performance may depend a lot of other jobs and even an entire enterprise. The problem then is not so simple as it seems and it is difficult to conceive of any reduction in those sociological and psychological factors which lead to the need of sedation, whether or not this need is satisfied.

The next point which is worth considering is whether most individuals suffering with anxiety or emotional strain are best advised to abstain from all therapy leading to sedation. Although this is indeed a medical problem and cannot be answered except after consultation with a competent physician, it seems likely that the barbiturates do a tremendous amount of good compared with the known harm which they produce. It is quite certain that, considered with other sedatives, they are far safer; and one can readily conceive of many serious complications if sedatives were entirely eliminated from medical practice.

The advocates of strict barbiturate control also cite the number of suicides from this drug as an argument. Is it not fairly well established that the determination to commit self-destruction precedes the selection of the means? If so, then the use of barbiturates rather than hanging or shooting oneself must certainly result in fewer suicides. The barbiturates are painless and also quite inefficient as compared with hanging and many persons are alive today who selected "sleeping pills" rather than a stout rope. To evaluate properly the "barbiturate evil" in this connection one would need figures to show whether the availability of these drugs leads to more or less successful attempts at suicides.

Our main objection to the statements widely disseminated concerning the barbiturates is the impression that is created that pharmacists are largely or wholly responsible for placing these drugs in the hands of the laiety. One need but visit the office of any one of thousands of dispensing physicians to find these drugs one of their principle articles of stock and they are given to the patient with just as little discernment as any pharmacist might possibly employ. This is considered by many as a physician's inalienable privilege and we will not argue this point. It must, however, be realized that here, too, is an important source of supply. A case in point may be of interest. Not long ago a relative who lived alone was found dead in bed and was presumed to have died of natural causes, at least so stated the certificate of burial. His personal effects, however, yielded an unlabeled bottle containing over one hundred barbiturate tablets which inquiry showed to have been given him by his physician. The circumstances surrounding his death made barbiturate poisoning a strong probability but no autopsy was performed. How different would have been the conduct of the case had the barbiturate been in

a stock package or in a prescription container. And yet other than to show equal responsibility on the part of physicians what sound reason could one use to castigate the physician and insist on an autopsy. The selection of a means of death was but an unimportant detail. How much better it was than as if mercuric chloride were used with its long drawn out agony and pain.

If barbiturate control is decided upon as a necessary course of action the realm of the physician must also be approached as well as that of pharmacy. This should be done not in the spirit of "name-calling" and "finger-pointing" but with the realization that it is indeed a joint problem. It would also be wise to recognize the problem in its broad aspects and not consider solely the excesses in the prescribing and use of these valuable drugs.

L. F. Tice

CLASSIFICATION AND HARDNESS OF GRANULATIONS

By Chester P. Baker and Dorothea J. Reilly *

THE consistent production of good tablets requires an expert knowledge of the characteristics of the granulations from which they are made. It was pointed out in the April, 1945, issue of the AMERICAN JOURNAL OF PHARMACY (1) that little has been published in the pharmaceutical literature on the physical aspects of tablet manufacture. We would like to call attention to certain phases of this subject, namely, Classification and Hardness of Granulations.

The meaning of the term hardness, as applied to granulations, is rather vague. An experienced tablet maker picks up a small amount of granulation, rubs it between his fingers, and knows whether it is too soft or too hard. He knows from the resistance to fracture and the feel of the fine powder produced, if he is likely to have trouble. He knows that a soft granulation, relatively free from fine powder, will often result in capping. He knows a granulation of moderate hardness, with a small proportion of fine powder, is not likely to cap. But what is a soft, or moderately hard, granulation?

Hardness has been variably defined as resistance to abrasion, to scratching, to penetration, to machining, to fracture, etc. The varied hardness measuring instruments and the difficulties ecnountered in attempting to define hardness, indicate that hardness is not a fundamental property of a material, but rather, a composite one.

None of the standard instruments for measuring hardness of solids lend themselves to the determination of the hardness of a granulation. In this case we are interested in the resistance of the granulation to fracture with the resulting creation of fine powder.

The rate of fracture produced by an automatic sieve shaker appears to show promise as a method of standardizing the evasive quality of hardness. The action produced by the sieve shaker on the granulation is not unlike that taking place during tablet manufacture up to the time the granulation is compressed.

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* From the Department of Research and Control, United Drug Company, Boston, Massachusetts.

The particle size distribution plays an important part in tablet production. The size classification of three typical granulations, made before running powders were added, is shown in Table I. A type H. L. Gyratory Laboratory Sifter manufactured by the Great Western Manufacturing Company was used to get the experimental data. (Fig. 1.) Weighings of the amounts left on each screen were made at the end of two, four, and six minutes.

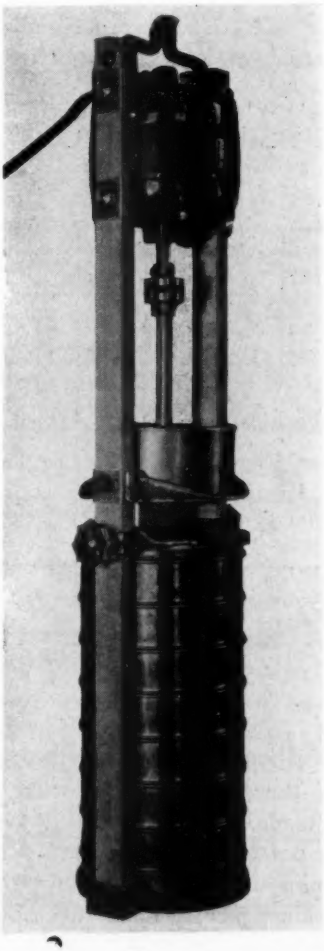

FIG. 1

TABLE I

Granulation: Acetphenetidin

Per Cent Left After Minutes				Per Cent Through After Minutes			
Mesh	2	4	6	Mesh	2	4	6
8	0.0	0.0	0.0	8	100.00	100.0	100.0
20	21.6	20.0	19.2	20	78.4	80.0	80.0
40	34.5	34.5	34.4	40	43.9	45.5	46.4
60	17.6	18.1	18.0	60	26.3	27.4	28.4
80	7.1	6.9	7.0	80	19.2	20.5	21.4
100	4.0	3.9	4.1	100	15.2	16.6	17.3
				120	13.2	14.5	15.2
Pan	13.2	14.5	15.2	Pan	0.0	0.0	0.0

Granulation: Sulfathiazole

Per Cent Left After Minutes				Per Cent Through After Minutes			
Mesh	2	4	6	Mesh	2	4	6
8	1.0	0.5	0.4	8	99.0	99.5	99.6
20	56.7	55.7	55.1	20	42.3	43.8	44.4
40	26.1	26.8	26.6	40	16.2	17.0	17.8
60	10.7	10.7	11.3	60	5.5	6.3	6.5
80	2.7	2.9	3.1	80	2.8	3.4	3.4
100	1.5	1.4	1.3	100	1.3	2.0	2.1
120	0.3	0.5	0.5	120	1.0	1.5	1.6
Pan	1.0	1.4	1.5	Pan	0.0	0.0	0.0

Granulation: Bisma Rex Mates

Per Cent Left After Minutes				Per Cent Through After Minutes			
Mesh	2	4	6	Mesh	2	4	6
8	0.2	0.1	0.1	8	99.8	99.9	99.9
20	42.5	42.0	41.5	20	57.3	57.9	58.4
40	24.7	24.7	24.8	40	32.6	33.2	33.6
60	14.1	14.1	14.2	60	18.5	19.1	19.4
80	6.6	6.3	6.4	80	11.9	12.8	13.0
100	3.2	3.4	3.3	100	8.7	9.4	9.7
120	1.9	1.6	1.8	120	6.8	7.8	7.9
Pan	6.9	8.0	8.1	Pan	0.0	0.0	0.0

A perfect classification cannot be obtained by this method since a certain amount of the granulation is being broken down as the separation is being made. It is noted, however, that a relatively small change in the per cent on each sieve occurred between four and six minutes running time. The per cent on each sieve at the end of six minutes presents a picture of relative amounts of granules of each size in the granulation.

The chemical and physical properties of the medicament and diluent, the binder used, the amount of moistening agent, and the skill used in granulating all contribute toward fixing the characteristics of the resulting granulation. Experience has shown that insufficient binder or too little moistening agent produces a fairly soft granulation. A size classification provides a means of control once a satisfactory formula has been worked out for a tablet.

It was noted that a perfect classification could not be secured using the gyratory sifter since a small amount of fracturing takes place as the classification is being made. The rate of fracture varies with different granulations. The harder granulations will have a smaller rate of granule size change than the softer granulations. This characteristic forms a basis for a method of determining the relative hardness of granulations.

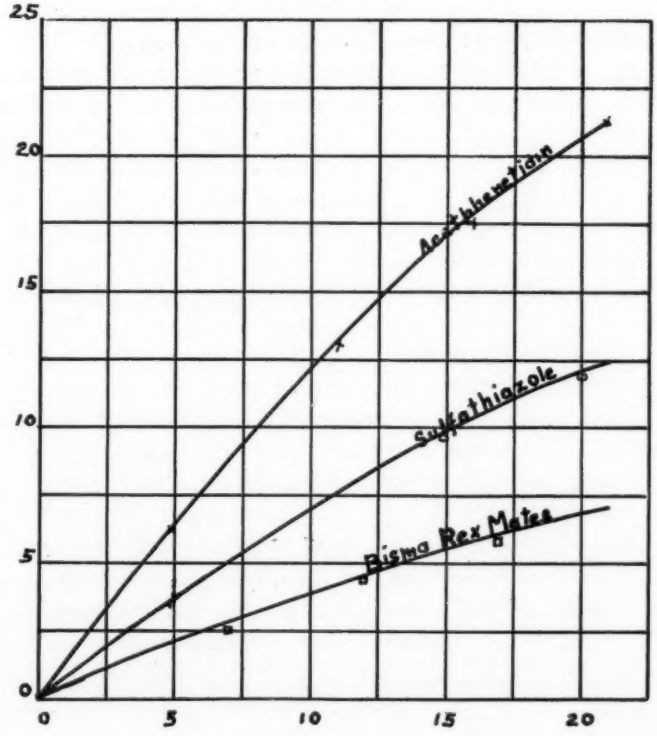

FIG. 2

Fig re 2 shows a series of three curves in which the per cent reduction in the portion of the granulation caught between the twenty and forty mesh screens at the end of ten minutes of classification was plotted against additional shaking time. Tests on a large number of granulations gave similar results. The granulations which were considered soft showed the greatest per cent reduction in the size of the granules. The granulations which were usually referred to as hard exhibited relatively less tendency toward breakdown, and consequently smaller rates of change of granule size.

This method presents a means of determining (1) the size classification and relative hardness of granulations, (2) the effect of varying the amount of moistening agent, and (3) the hardness produced by different binders on the same material.

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AN EXPERIMENTAL STUDY OF THE PHOTOCHEMICAL DESTRUCTION OF PYRIDOXINE HYDROCHLORIDE (VITAMIN B_6)*

By Harold C. Epley

THERE has been much less reported on the stability of Pyridoxine Hydrochloride than on other isolated Vitamins.[1] Keresztesy and Stevens [2] reported that Pyridoxine and Pyridoxine Hydrochloride sublime without decomposition, are stable toward concentrated hydrochloric acid at elevated temperatures, are not affected by heating with alkalis, nitrous acid, ethyl nitrite or Fehling's solution. They are, however, destroyed by light.[3-4] Hochberg, *et al.*[5] reported that Pyridoxine Hydrochloride was rapidly destroyed by light in neutral and alkaline solution but that it was stable toward light in 0.1N hydrochloric acid (pH 1).

There have been no reports upon the effect of the wave length of light upon the rate of the photochemical destruction of Pyridoxine Hydrochloride, nor upon the protection offered by bottles of various colors.

This study was divided into two parts. One, solutions of Pyridoxine Hydrochloride (25 gammas/cc.) were exposed to artificial light through filters of various colors and the destruction measured. Two, solutions (45 gammas/cc.) were exposed to diffused daylight (approximating storage conditions in the average drug store) after being placed in bottles of various colors.

In the first part of the study, the solutions of Pyridoxine Hydrochloride, in a 150 cc. pyrex beaker, were placed in a light-tight box and exposed to the light of a 300-watt bulb in an aluminum reflector placed at a distance of 8 inches from the beaker. Exposures were made through filters of various colors placed over an opening of 1½ inches in diameter in the box.

Inasmuch as the solutions were in an uncovered beaker, there was considerable evaporation with consequent concentration especially with no filter over the opening in the box. Hence, factors had to be determined to compensate for the evaporation.

*Presented in partial fulfillment of the requirements for the degree of M. Sc. in Pharmacy, University of Southern California.

The characteristics of the filters were obtained in the log scale.[6] These were transposed into the arithmetic scale and the inherent opacity of the filters to the color of light passed was determined.

In determining these factors, the following divisions of color were used:[7]

Blue Light	(Violet and Blue)	400-500 mu
Green Light	(Green and Yellow)	500-600 mu
Red Light	(Orange and Red)	600-700 mu

Gettman and Daniels[8] give the peaks of color in terms of wave length (in millimicrons) as follows:

Violet	420;	Blue	470;
Green	530;	Yellow	580;
Orange	620;	Red	700.

Using the above divisions:

Wratten Filter C-5	(Blue)	passes 39%	Blue Light
Wratten Filter X-2	(Green)	passes 55%	Green Light
Wratten Filter K-2	(Yellow)	passes 81%	Green Light
		86%	Red Light
		7%	Blue Light
Wratten Filter A	(Red)	passes 80%	Red Light

The following filter factors were used:

Wratten Filter C-5	(Blue)	39%
Wratten Filter X-2	(Green)	55%
Wratten Filter K-2	(Yellow)	85%
Wratten Filter A	(Red)	80%

Concentrations of Pyridoxine Hydrochloride were determined by the colorimetric method of Scudi.[9] This is based upon the color reaction between Pyridoxine and 2,6-dichloroquinone-chloroimide, adjusted so that determinations may be made on solutions containing 1 to 10 gammas per cc. The mechanism of the reaction appears to be that found for the indophenol reaction in general. The color will develop only in a slightly alkaline solution (pH 7.6) but the pH must be carefully controlled to prevent the decomposition of the indophenol in alkaline solution.

Procedure: To 1 cc. of Pyridoxine solution add 10 cc. of a solution of 2,6-dichloroquinone-chloroimide * and 3 cc. of Veronal buffer ** pH 7.6. Shake. Let stand ten minutes. Shake. Let stand ten minutes. Centrifuge. Read color on photo-electric colorimeter using a red (660 mμ) filter.

The results indicate that photochemical destruction becomes progressively more rapid as the wave length of the light decreases, although there is apparently destruction by light of all colors.

The brown bottle gave the most protection, the green bottle was next in effectiveness while the blue bottle was only slightly superior to the white bottle. The control, a solution of Pyridoxine Hydrochloride kept in total darkness, showed gradual decomposition, although slower than any of the solutions exposed to light. A sample of a commercial Vitamin B-complex preparation (an extract of rice polishings, fortified by synthetic factors, in a wine base) purchased on the open market, that had been stored under normal conditions in a drug store, showed a Pyridoxine content equal to label claims. Hochberg, *et al.*[1] reported Pyridoxine to be stable in multivitamin preparations.

It thus appears that although Pyridoxine is relatively stable in commercial Vitamin B-complex preparations from natural sources if kept in darkness, Pyridoxine Hydrochloride itself is apparently unstable in solution even in total darkness.

The results indicate that colored bottles, especially brown bottles, offer protection to Pyridoxine Hydrochloride in solution. It is, however, recommended that Pyridoxine Hydrochloride be packaged in the dry state and not dissolved until shortly before use.

CONCENTRATION OF PYRIDOXINE HYDROCHLORIDE IN SOLUTION

(Following Exposure to Diffused Daylight)
In Colored Bottles (gammas/cc.)

Exposure in Weeks	0	1	2	4	6	8	11	16	18
White Bottle	45	42	41	37	37	24	14	10	10
Blue Bottle	45	34	37	34	32	28	15	13	13
Green Bottle	45	38	42	40	38	33	21	19	16
Brown Bottle	45	37	37	37	35	34	24	26	27

* 100 mg. 2,6-Dichloroquinone-chloroimide (Eastman #2483) dissolved in 1600 cc. of acid-free, reagent N-butanol.

** 15 gm. sodium diethylbarbiturate dissolved in 700 cc. distilled water. Titrate to pH 7.6 with dilute HCl using glass electrode pH meter. Filter off the precipitated diethylbarbituric acid.

CONCENTRATION OF PYRIDOXINE HYDROCHLORIDE IN SOLUTION

(Following Exposure to Artificial Light Through Various Filters)

Corrected for Inherent Opacity of Filters (gammas/cc.)

Exposure in hours	0	20	40	60	58	66
No Filter	25.0	15.0	11.0	7.5	4.5	
Blue Filter	25.0	19.1	14.0	9.6	6.2	3.4
Green Filter	25.0	21.4	18.8	16.8	15.0	13.0
Yellow Filter	25.0	21.5	18.8	16.8	15.1	14.0
Red Filter	25.0	23.1	21.9	20.9	20.0	19.5

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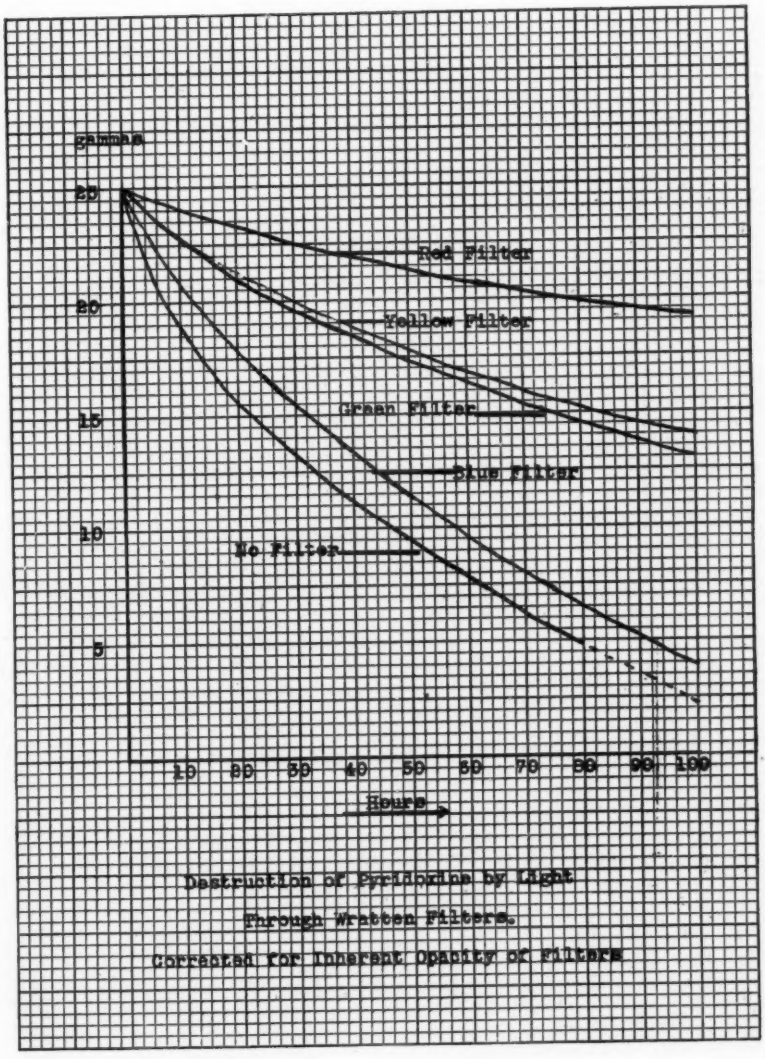
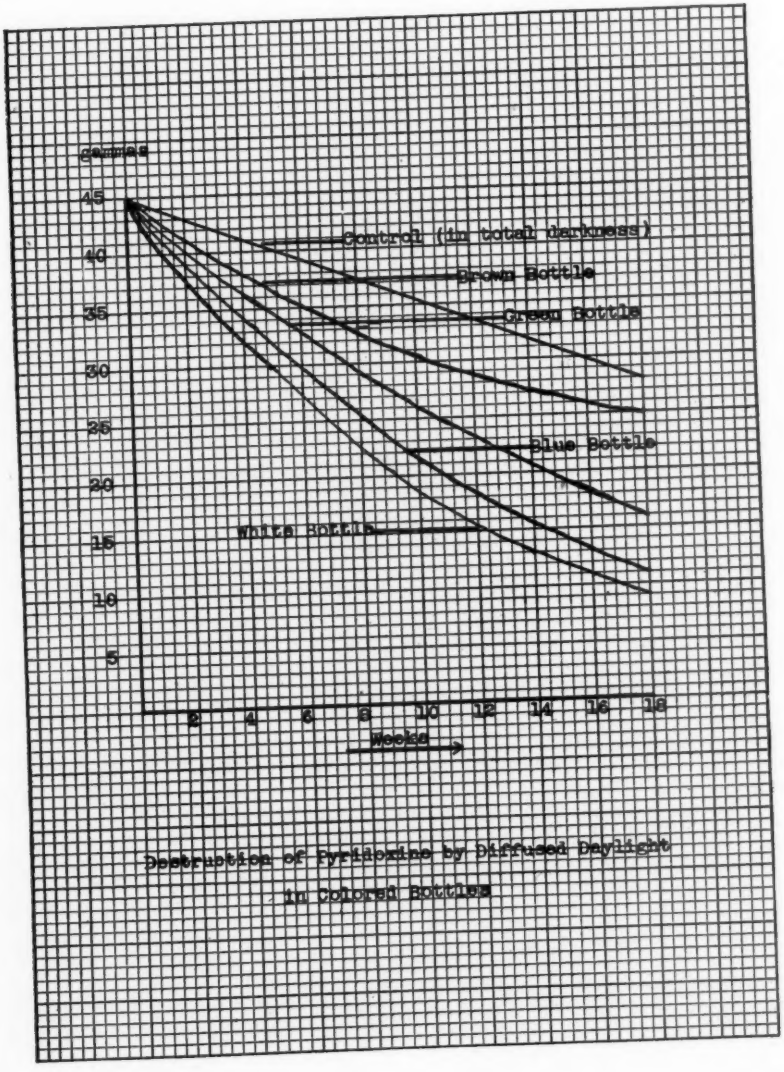
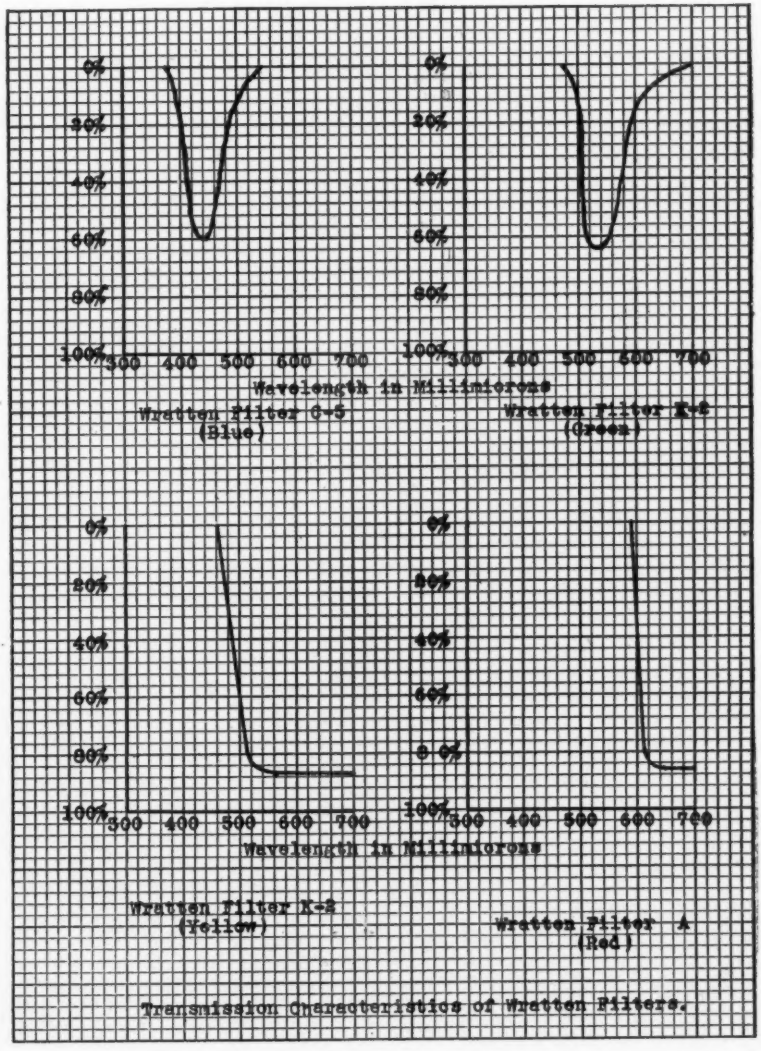


Destruction of Pyridoxine by Light
Through Wratten Filters.
Corrected for Inherent Opacity of Filters



Destruction of Pyridoxine by Diffused Daylight in Colored Bottles



Transmission Characteristics of Wratten Filters.

PREPARATION OF A PENICILLIN LOZENGE

By J. A. Nussle *

IT has been established that penicillin, in order to be effective as an antibacterial agent, must come into direct contact with the sensitive organisms for an appreciable length of time. In certain types of infection, as in diphtheria, the bacteria are found on the surface of the mucous membranes and do not enter the general circulation. For this reason local treatment which would maintain contact of the penicillin with these organisms for a considerable period promised to be more effective than parenteral administration of the drug. With this in mind, at the suggestion of the medical service of the hospital, we undertook to develop a lozenge containing penicillin in a sufficient concentration to release an effective dosage over a period of between fifteen and twenty minutes. Such a lozenge could be held in the mouth until totally dissolved and repeated at frequent intervals. In this way the antibacterial action of the penicillin against the offending organisms upon the mucosa of the mouth and throat could be effected. In addition the medical service deemed it advisable to supplement the action of the lozenge by nasal spray with a penicillin solution. The experiments in connection with the development of the lozenge are here recorded and two satisfactory methods for their preparation are given.

Necessary Qualities of Lozenge Base

In considering the development of a lozenge base suitable for the preparation of a penicillin lozenge several factors had to be kept in mind. First, the base must be one which will slowly dissolve in the saliva when held between the tongue and hard palate, thus slowly and steadily releasing the penicillin into solution in the saliva for local action upon the surface membranes of the mouth and throat over a moderately long period of time. In this study about 15 minutes was considered to be the optimum time for complete solution of the lozenge in the mouth.

Secondly, the finished lozenge base must be such that it remains sufficiently fluid to pour at temperatures down to between 60 and 70

* Technical Sergeant, U. S. Army Medical Department.

degrees Centigrade. This permits admixture of the freshly prepared, concentrated solution of the penicillin with the lozenge base just before pouring and chilling it to form a mat which can be cut into a number of individual lozenges. In this way deterioration of the penicillin from subjection to excessive heat is avoided. This factor must be considered when the lozenges are made in large numbers for use on the wards, due to the fact that the need for them sometimes fluctuates, thus necessitating that they be stored for a considerable time before the entire lot has been used. Caution in the matter of exposure of the penicillin to heat during the production of the lozenges and storage of the product in the refrigerator maintains a high potency of the lozenge, so that some loss of activity may occur during storage without interfering with the therapeutic efficiency.

Thirdly, the taste of the lozenge must be considered. It can readily be seen that an unpleasant taste or flavor would cause the patient to chew the lozenge in order to be rid of it more quickly or to spit it out after only a few seconds' time. Therefore, the finished lozenge must have a pleasant taste and flavor; yet one must avoid adding anything for flavoring which would cause or hasten deterioration of the penicillin.

Fourthly, in war time it is necessary to consider the availability of ingredients and equipment necessary in the preparation of the product due to the limited variety and amounts of some materials obtainable under the circumstances.

Relative to the stability of the penicillin during storage of the lozenge, tests run through the kind cooperation of Captain Morris of our laboratory service give some indication that the lozenge retains satisfactory penicillin antibacterial activity for two to three weeks when refrigerated at a temperature of 5 degrees Centigrade.

Formulae Studied

The first material tried as the basis of a gel for the preparation of the lozenge base was gelatin. Since a plain gelatin-water gel is much too soft and quickly dissolved in the mouth, a number of formulæ were worked out and tried using Glycerinated Gelatin as the primary ingredient. Table I shows the percentage by weight of the various ingredients in each formula and the findings as to the suit-

Note:—Information on the indication and directions for use of this mode of penicillin therapy will be available through a medical paper by Colonel Rudolph A. Kocher.

TABLE I. RESULTS IN STUDY OF VARIOUS FORMULAE USING GLYCERINATED GELATIN AS PRIMARY INGREDIENT.

Trial Formula Number	Ingredients and Weight Percentage of Each in the Formula						Dissolving Time on Tongue in Minutes	Properties and Suitability of the Lozenge Base
	Gelatin	Glycerin	Starch	Sucrose	Agar	Water		
1.	15.	10.	5.	20.		50.	6 minutes	Gel too soft; dissolves too quickly on tongue. Moldy even though refrigerated.
2.	16.5	16.5	6.			60.	8 minutes	Gel too soft; dissolves bit too quickly on tongue. Moldy even though refrigerated.
3.	22.	28.	10.			40.	12 minutes	Good gel—proper consistency, but becomes moldy even though refrigerated.
4.	5.5	5.5	1.5	55.		32.	6 minutes	Not complete gel; too soft and gummy, making it impossible to cut mat into lozenges.
5.	10.	25.			0.5	65.	5 minutes	Gel much too soft.
6.	15.	40.			1.0	44.	7 minutes	Gel a bit too soft.
7.	20.	53.			2.0	25.	10 minutes	Gel satisfactory for lozenge base, but somewhat disagreeable granular taste.
8.	50.	50.					10 minutes	Gel satisfactory for Lozenge Base.

ability of the resulting gel for the preparation of the lozenge. Using these formulæ it was found that a plain Glycerinated Gelatin is the most suitable as a base for the preparation of a penicillin lozenge.

The official U. S. Pharmacopœia formula for Glycerinated Gelatin was used:

Gelatin (sheet or granular)		800 Gm.
Glycerin		640 cc.
Penicillin		400,000 Units
Sterile Distilled Water		20 cc.
	To make	400 Lozenges

(Each lozenge averages 4 Grams weight and 1000 Units penicillin content.)

Method of Preparation

Pour upon the gelatin sufficient distilled water to cover it. (If granular gelatin, dust the gelatin slowly into the distilled water, adding more water as needed until all the gelatin has been wetted.) After allowing the gelatin to soak for about 15 minutes, pour off excess water. Place the glycerin in a tared dish of about 2000 cc. capacity and add the wetted gelatin. Heat the mixture on a water bath until the gelatin is dissolved and water evaporated off to make 1600 grams of product. Remove the dish from the heat and allow the glycerinated gelatin to cool. Meanwhile make a solution of the penicillin in about 20 cc. of sterile distilled water. When the gel has cooled to about 65 degrees Centigrade, stir in the solution of the penicillin to obtain a uniform mixture. Immediately pour the mixture into a suitable sized tray and refrigerate it on a level surface to form a mat of uniform thickness. Cut the mat into 400 equal sized lozenges and store them at a temperature of 5 degrees Centigrade.

To form the mat and cut it into lozenges we use a specially constructed tray built of plywood and nailed flat on a heavy wood base. The side walls are 1 inch high and are set firmly onto the bottom piece without any cracks at the corners. The bottom piece is 16 inches square and is ruled with guide lines four-fifths inch apart in both directions to facilitate cutting the mat into 400 lozenges.

Preparation Using Agar Gel

After a short time it was found that although Glycerinated Gelatin formed a fine lozenge base, it carried with it the disadvantage

that the ingredients were of limited availability to us. Therefore, work was undertaken to develop a suitable base using agar as the primary ingredient of the gel.

Since a plain agar gel is very friable and practically insoluble in the saliva at mouth temperature, it was necessary to experiment with the addition of other materials of such a nature as would render the gel cohesive and of satisfactory solubility in the saliva. With this in mind several combinations of agar, simple syrup, glycerin, starch and glycerite of starch were tried. Table II shows the findings as to the results with the various formulæ tried in this part of the study.

It will be noted that both Formula No. 11 and Formula No. 15 gave satisfactory gels for a penicillin lozenge base. Formula No. 15 contains the same percentages of starch and glycerin as does Formula No. 11, the difference being that these two ingredients are made into Glycerite of Starch before being mixed with the other ingredients in the former. By experience it was learned that Formula No. 15 produced a finished lozenge of somewhat more satisfactory solubility in the mouth.

Therefore, from among the various formulæ tried in this part of the study the following was selected as the most satisfactory for an agar gel lozenge base:

Agar, granular		30 Gm.
Simple Syrup		875 cc.
Glycerite of Starch		350 Gm.
Penicillin		400,000 Units
Sterile Distilled Water		20 cc.
	To make	400 Lozenges

(Average lozenge weighs 4 grams and contains 1000 Units of penicillin.)

Method of Preparation

Prepare the Glycerite of Starch by the official method. After obtaining the proper weight of Glycerite and while it is still hot, slowly add the syrup in small portions with thorough stirring to produce an even mixture. Transfer the mixture to a wide-mouth, heat-resistant container of about 2000 cc. capacity. Dust the agar in small quantities onto the mixture and stir it in, taking care to avoid lumping of the agar. Cover the container with several layers of gauze and autoclave at 15 pounds pressure for 20 to 30 minutes to obtain com-

TABLE II. RESULTS IN STUDY OF VARIOUS FORMULAE USING AN AGAR GEL AS THE PRIMARY INGREDIENT.

Trial Formula Number	Ingredients and Weight Percentage of Each in the Formula: Agar	Simple Syrup	Glycerin	Starch	Glycerite Starch	Dissolving Time on Tongue in Minutes	Properties and Suitability of the Lozenge Base
9.	1.75	98.25				7 minutes	Gel too brittle—poor cohesion, so that the lozenge breaks into pieces on the tongue.
10.	2.5	97.5				27 minutes	Gel too hard and brittle. Lozenge breaks into pieces and dissolves very poorly.
11.	2.0	75.	20.	2.4		15 minutes	Gel has good cohesion and lozenge dissolves well on tongue. Glycerin and Starch promote slow, uniform solution of lozenge.
12.		60.			40.		No gel.
13.		50.			50.		No gel and pronounced, disagreeable starchy taste.
14.	1.0	76.			23.	¼ minute	Gel too soft; no cohesion.
15.	2.0	75.			23.	20 minutes	Very satisfactory gel—proper cohesion, firmness and slow, surface solution of lozenge on the tongue.
16.	3.0	74.			23.	30 minutes	Satisfactory gel—good cohesion, but a bit too slow solution of lozenge on the tongue.

plete solution of the agar. (While the pressure in the autoclave is falling, prevent it from dropping too rapidly in order to avoid having the mixture boil out of the container.) Remove the mixture from the autoclave and allow it to cool to 70 degrees Centigrade. Dissolve the penicillin in the sterile distilled water and stir it thoroughly through the lozenge base to obtain uniform distribution. Immediately pour the mixture into a suitable sized tray and refrigerate it on a level surface, forming a mat of uniform thickness. Cut the mat into 400 lozenges and store them in the refrigerator.

Summary

(1) The rationale of the use of a Penicillin Lozenge to obtain the action of this antibacterial agent upon the mucosal surface of the mouth and throat in certain types of infections is briefly discussed.

(2) The necessary qualities of a satisfactory base for a Penicillin Lozenge are reviewed.

(3) Two formulæ and methods for the preparation of a Penicillin Lozenge are presented. The first is a Glycerinated Gelatin base; the second is a gel prepared from Agar, Simple Syrup and Glycerite of Starch.

SOME SCIENTIFIC IGNORANCE

By T. Swann Harding *

Editor's Note—The following article by Mr. Harding is almost certain to produce in the reader either strong endorsement or strong resentment. Few indeed will read it with no flurry of reaction. Although Mr. Harding questions the "social-efficiency" of some of our corporations, he does not offer any clear-cut alternative which is likely to provide great improvement. We believe the author to be quite sincere in his beliefs and for that reason, if for no other, he deserves space to present his views. No one can deny his ability to write in an interesting and challenging manner, even though one may oppose his arguments.

AN odd exhibition of scientific ignorance cropped up recently in a news bulletin emanating from the American Association for the Advancement of Science. F. R. Moulton, one of the Association's college of cardinals, felt called upon to defend corporate monopolies. He performed this feat in an editorial leader entitled "The Middle Man," adopting the familiar device of making huge corporations over into street-corner grocers, and portraying them as the defenders of widows and orphans.

It required considerable contrivance to defend this thesis, but brother Moulton managed very well. However, he thereby displayed the traditional ignorance of physical and biological scientists regarding those mysterious disciplines subsumed in the categories of economic and social science. The weaklings for which he went to bat were Swift & Co. and General Motors. He proved to his own evident satisfaction that both were magnificently efficient social service institutions.

To wit, Swift, in 1943, paid out 77.7 cents of every dollar it took in to farmers and growers of livestock. Here was proof positive of its singular nobility of character. After deducting its other expenses, Swift had but a trifling 0.6 cent per dollar of intake as a reward for its risk-bearing stockholders. Moulton asserted categorically that Swift's figures were correct in every minute detail, and that its operations were quite similar to those of all other large food concerns.

Next he remarked that General Motors, out of the billions of dollars it took in during 1943 (mainly or wholly from government),

* Granite Gables, 400 Linden Lane, Falls Church, Va.

paid out only 2.3 cents per dollar to holders of its common stock. In fact it had to reserve three times as much to meet taxes as to pay dividends. Half of its stockholders also were women, many of whom had invested their life savings in its stock.

Indeed 80 per cent of those who shared this annual melon of $87,100,000, owned as much as 1 per cent. True, the duPont Company owned a huge block of the stock, but even it munificently distributed the dividends therefrom among its own stockholders. Moulton finally declared that all huge corporations were amazingly efficient in operation and offered the finest investment opportunities.

Publication of this item provoked a flurry of letters, many of them opposed, which remained unpublished. But one wonders why the American Association for the Advancement of Science would want thus officially to defend corporate monopoly. It is doubtless true that many such corporations are highly efficient profit-producing units when selling to government in wartime. But the intelligent question to ask is whether they are socially valuable institutions.

While Swift, like other food concerns, naturally must make heavy payments to farmers every year, have those payments been as large as they should have been to ensure farmers decent living standards? While such concerns may have been efficient enough to produce food at low rates of profit per pound, could this profit reasonably have been lower? Were production economies passed along to consumers in the form of lower prices? Would it have been possible to supply even better foods at still lower prices?

The distinguished agricultural economist, O. E. Baker, has estimated conservatively that, in the period of "prosperity" between 1920 and 1929, rural people made a net contribution of over twenty-five billion dollars to urban people. During this same period our basic producers of food and fiber served the rest of us at a 40 to 60 per cent discount. This they did by depleting their farm plants and working at starvation wages. Was that as it should have been?

It left farmers quite generally bankrupt. One reason for this was that they had to take what was offered for their products by huge food concerns and others buying at wholesale, while farmers purchased their supplies and equipment at retail. When, in 1933, an average city family spent $264 per year for food, the farmer got only $92 of that. Was that sufficient? Was the nine cents out of the dollar consumers spent for wheat cereals equitable reward for the

basic producer? Did farmers get what they should have received for livestock?

In those days one-fourth of the farm families that were not on relief (and plenty were on relief) had inadequate diets. Such dietary deficiencies are also commonly found in every survey of the nutritional condition of rural people up to the present. Whatever the prices paid farmers, they have, until recently, been insufficient to enable them to maintain a decent American standard of living, and even during wartime not all farmers cleaned up.

The question is not so much what Swift or any other company makes or pays out as dividends. It is whether that much is too much when society is considered as a whole. Moulton claimed that the packers acted quite like other large food concerns. Then what is their social efficiency?

Is all their expensive advertising, processing, packaging, and so on, justified? What about the vertical integration of vast corporate chains which both wholesale and retail foods, and also control warehouses, canneries, bakeries, milk plants, meat-packing plants, coffee-roasting establishments, general factories, and even printing plants? What is the effect of this upon our society and our economy?

What has been the social effect of having four huge packers control meat and related lines? In 1940 also six large dairy establishments, four of which were national in scope, controlled the butter, cheese and condensed milk fields. Two or three large concerns controlled the major part of the flour-milling, bakery and biscuit businesses. Similar conditions existed in the canning field.

Were the advantages of consolidation as fully passed along to consumers in reduced prices as they should have been? Were some of these concerns actually too large for economical operation? For a point can be reached where the inherent inefficiencies of mere bigness prevent effectual operation. Finally, are profits what they should be, all social factors being considered?

Incidentally the above-mentioned farmers met this thing head on, for three large firms controlled 92 per cent of the business in binders; one firm alone controlled 56 per cent. Three firms controlled 76, and one alone 56 per cent of the tractor business. Did this conduce to lowered costs of farm operation and enhanced farmer income?

The growth of monopolies undermined the traditional concept of competitive enterprise. The economies effected by large units result from the operating advantages and the rationalization of marketing which follow upon the scientific integration of related lines. It is also true that large concerns do tend, at least to a certain point, to give better service and pay higher wages than small ones. But do they go as far as they should in these directions?

Again, it is quite well-known that large food concerns constantly glorify perfectly ordinary products, often processing much of the nutritive value out of them for the sake of appearance. Then, by expensive advertising, for which consumers unwittingly pay, they prevail upon the public to expect and to finance a great deal of superfluous processing, packaging and other pseudoservices. Is such procedure socially beneficial?

Turning to General Motors we find Moulton strangely silent about the fact that, in November, 1939, the Federal Trade Commission forbade this company's subsidiary, the General Motors Acceptance Corporation, to use the expression "6 per cent" in any form in advertising its installment car-purchase plan. For the advertising led unwary consumers to believe they would pay only 6 per cent on the unpaid balances of their loans, whereas the interest was often 8 or even 12 per cent in reality.

A corporation that would stoop to so cheap a trick leaves something to be desired from the standpoints of ethics and social values. Then, in April, 1942, Judge Vincent L. Liebell, of the United States Circuit Court in New York, decided that eight General Motors executives should reimburse the concern in the amount of $4,348,044, plus interest charges of $2,000,000 more. He held that they had breached their fiduciary trust to the stockholding widows and orphans. But Moulton does not mention this occurrence.

What had transpired, said the Court, was an unauthorized distribution of stock, a waste of corporate assets, with improper management of bonus funds. The suit had been brought by minority stockholders who resented such high-handed actions of the executives. It was proved that the bonus plan approved by the stockholders had been violated. No such firm can honestly be regarded as socially efficient, however great its economic stability.

But how great is that? In the latter 1930's General Motors was paying its workers an average of $1,100 a year. That would

have barely sustained a family, if paid regularly, which it was not, for shut-downs occurred. Workers were then expected to go on relief. In having such expectations General Motors was in no sense peculiar. Most big concerns expect the community to pauperize them by maintaining their labor pools in times of adversity.

The community also bears, rears, educates or imports this labor pool. But industry expects it to reassume responsibility for the workers immediately production slackens. Such charges for relief should appear in company budgets under cost of operation, but they do not, because private enterprises practice double-entry bookkeeping. Thus they mask the fact that they quite commonly depend upon private charity or government doles for profit maintenance.

The entire automobile industry could not have been the outstanding success it turned out to be had not government financed the construction of billions of dollars worth of roads. Indeed the industry depended upon government for basic research on roads, tires, soils and the effects of wheel impacts on roads of different types.

American private industry generally has had tariff favors, direct subsidies, low-cost loans, licenses, patents, monopoly grants, government orders, indirect subsidies, and even actual treasury doles. Are our private industries solvent or are they not? What moral right has a corporation to pay any dividends at all until it has fulfilled its social obligations and expunged its debt to the community which prospers it?

Very often the most successful corporation is the one which most completely unloads its obligations on the government or the local community. A plant may be an efficient money-making and dividend-paying institution though it renders scant public service and even if it does cast its employees out on charity immediately its sales shrink. It may pass along to its clientele, in the form of lowered prices, some of the advantages it enjoys by escaping its obligations.

But is it, in last analysis, a useful social institution, except as recent tax policy has compelled it to disgorge somewhat? Moulton says the big monopolies support women with stock dividends. Who gets those dividends? Two or three years ago there were only about six million stockholders in the entire nation, of whom 75,000 owned one-half of all corporate stock, and 300,000 three-quarters of it. Is that widespread dispersal of corporate ownership?

In 1935 also a scant 0.3 per cent of our 475,000 corporations received 62 per cent of the corporate net income. Through interlocking directorates these giants just about controlled all corporate business of the United States. The thousand corporations standing next below the giants received nearly all the rest of the corporate net income reported. Is that good economics? Investigation has shown that a scant 5 per cent of the stockholders of American Tel. and Tel. owned over half its stock in 1935. These big fellows and their proxies easily perpetuate their control over the policies of such corporations. Is that socially beneficial?

We should endeavor to measure the social performance of our corporations scientifically. If our scientists were alert this might be done. In doing it such questions as these should be answered:

How much employment does the corporation provide? What is its total output? What is the actual cost, including hidden costs, of its output to society as a whole? What happens to the money, every cent of it, which the corporation takes from consumers? How big is its payroll and just what does it expend for wages, interest, materials and dividends? What quality goods and services does it provide, and could these be better provided otherwise?

Answers to these questions might get us somewhere. The American Association for the Advancement of Science should interest itself in this research instead of blindly defending monopoly. Thus it has been estimated that if all industries had operated with the social efficiency of agriculture during the 1932-33 period we should have had only two million unemployed. But had they operated only with the social efficiency of American Tel. and Tel., which fostered technological unemployment right and left, we should have had nineteen million unemployed.

During the pre-war period American industry was characterized by a level of production which constantly outran the level of employment and of consumer purchasing power. The consumer funds employed by industry tended to outrun production. Dividends and interest payments tended to outrun payrolls and the national income. That was bad economics.

While we were at peace a substantial part of our industry worked towards producing more and more while using less and less labor. It took more and more purchasing power from consumers in ex-

change for less and less goods and services. It paid less and less to labor and more and more to stockholders and bondholders.

The fact that agriculture operated with relatively high social efficiency penalized it severely in an openly riotous pecuniary economy. That is why it failed to fit into the national industrial picture. That is why farmers were caught in a squeeze. That is why, after 1933, we paid farmers back a small part of the billions they gave freely to others during the era of false prosperity.

True enough, financial and industrial management accomplished its major obligation to ownership. It produced profits. But at what social cost? At what cost in exploitation of our natural and human resources? It failed to meet reasonable social performance tests. The American Association for the Advancement of Science to the contrary notwithstanding, that is what must count most in the post-war period if the United States is to have real prosperity.

SELECTED ABSTRACTS

Effect of Acid Beverages Containing Fluorides Upon the Teeth of Rats and Puppies. J. S. Restarski, R. A. Gortner and C. M. McCay. *J. A. D. A. 32,* 668 (1945). A popular soft beverage of the "cola" type was found to have a destructive effect upon the enamel of the molars of white rats and the deciduous teeth of puppies when consumed for periods of five days or more by the former animals and three weeks by the latter.

Chemical analysis of this beverage showed that it contained 10 per cent by weight of sucrose and 0.055 per cent of phosphoric acid (H_3PO_4). Its pH, determined electrometrically, was 2.6.

The substitution of a prepared solution with the same sucrose and phosphoric acid concentration and the same pH as the commercial beverage produced similar destruction of the enamel. A saccharin and phosphoric acid solution of equal sweetness and acidity was found to be much less destructive than the preparation containing sucrose.

When 0.15 per cent of methocel was added to the saccharin-acid solution in order to render its viscosity equal to that of the sucrose-acid preparation, the former beverage was found to be but little more destructive to the molars of rats than that which contained only saccharin and acid.

Rats or puppies which were fed a 10 per cent sucrose solution were found to have a normal enamel surface on the teeth. The aggravation of the action of acid on teeth by the presence of sucrose is of interest, and the study is being extended to include carbohydrates other than sucrose.

The inclusion of from 1 to 20 parts per million of fluorine (as sodium fluoride) in either the "cola" or the sucrose-acid beverage considerably decreased, but did not prevent completely, the destruction of the enamel in rats or puppies.

The observations suggested that the sodium fluoride acted directly upon the enamel surfaces as the beverage came in contact with the teeth, since all rats and puppies, whether used as test animals or as controls, received throughout the entire series of experiments a commercial dog food which contained 20 parts per million of fluorine.

The authors do not consider that any conclusions drawn from these data can, at present, be extended to include man, since the manner of drinking, the relative amount of saliva and its buffer capacity, and probably other factors, are different in man from what they are in the animals studied.

Solutions of Adrenaline. G. B. West. *Pharm. J. 101,* 86 (1945). The B. P. 1932 and its Addenda do not permit the use of chlorbutol, cresol, phenol or sodium bisulfite as a preservative in solutions of organic substances intended for parenteral administration, although the U. S. P. allows the use of these substances in concentrations up to 0.5 per cent.

In 1939 the Committee on Pharmacy and Pharmacognosy of the British Pharmacopœia Commission recommended the addition of sodium metabisulfite to the official adrenaline solution.

The stability of adrenaline solutions under various conditions of pH and heating, both with and without sodium metabisulfite, was studied. The potency of the samples was determined physiologically on the isolated perfused frog heart and chemically by the method of either Folin and Ciocalteu or Folin and Dennis.

The optimum conditions found for stability and storage of solutions of adrenaline in hydrochloric acid contained in ampuls with a small volume of air were a pH of about 4.2 and the presence of 0.1 per cent of sodium metabisulfite. Such a solution, however, had a pH of about 3.1, and the use of less acid resulted in rapid oxidation.

This observation led to studies on the stability of adrenaline acid tartrate solution (1 in 1000 of the base) with 0.1 per cent sodium metabisulfite. This was found to have a pH of about 3.7, a value which decreased following heating or storage. This solution was found to be at an optimum for the effect of both heat and oxygen, since the loss of activity after autoclaving was negligible.

Studies were made of the effect of sodium metabisulfite on the toxicity of solutions of different adrenaline salts. Addition of the metabisulfite to unheated adrenaline hydrochloride solutions increased the toxicity to rats and mice and also speeded up the time of death, but such increases were not observed when the two substances were heated together prior to injection.

The presence of the metabisulfite in unheated solutions of adrenaline acid tartrate did not appear to influence toxicity in the rat. The approximate LD 50 for adrenaline as the acid tartrate agreed with the value found for the hydrochloride (6.83 mg. per Kg.).

Liquor Chloroxylenolis and Castor Oil Soaps. A. Firth. *Pharm. J. 100,* 318 (1945). Liquor Chloroxylenolis, Sixth Addendum to the B. P., is an antiseptic containing 5 per cent of *p*-chloro-*m*-xylenol in a saponaceous base made with ricinoleic acid and triethanolamine. Upon storage under various conditions the product separates into a thin, colored upper layer and a paler, jelly-like lower layer.

Studies made on the preparation have shown that it becomes cloudy with a rise in temperature to 90-100° F. A decrease in temperature to near the freezing point produces a more pronounced cloudiness and the deposition of soap which, however, may be redissolved by warming and agitation.

The upper layer was found to yield a blue color with bromothymol blue, and was more alkaline than the lower layer. The finished product should yield a blue green with bromothymol blue (pH 7-8). It was found that if the solution is adjusted to pH 6, which may be accomplished by reserving double the stipulated portion (6 mils) of the ricinoleic acid and alcohol mixture during the process of manufacture, the finished product will withstand almost freezing temperature.

The author advocates the use of a standardized castor oil soap containing 30 per cent w/v of fatty acids for convenient use in the preparation of official formulas, since it is readily miscible with water, alcohol and cresol.

The Benzyl Ester of Penicillin. C. J. Cavallito, F. K. Kirchner, L. C. Miller *et al. Science 102,* 150 (1945). Benzyl penicillin G was obtained as a colorless, hard glassy solid by treating free penicillin in an inert organic solvent with an excess of phenyl diazomethane. Any unreacted penicillin was extracted with sodium bicarbonate solution. Evaporation of the solvent yielded a resinous product which was readily purified.

Benzyl penicillin is soluble to the extent of approximately 2.5 per cent in sesame oil or propylene glycol. It is also soluble in alcohol, ether, chloroform, ethyl acetate and the polyethylene glycol type of polymers. It is stable at temperatures above 100° C., and it is much more stable in alcoholic solvents than any known penicillin salt.

In vitro, pure benzyl penicillin has about one-thirtieth the bacteriostatic activity of pure sodium penicillin against broth cultures of *Staphylococcus aureus* when tested by the serial dilution method, and only one four-hundredth by the cup-plate method.

The comparative protection afforded to mice inoculated intraperitoneally with *Streptococcus hemolyticus* (Strain C 203) by graded doses of both crude and pure benzyl penicillin in sesame oil and by sodium penicillin (1600 μ/mg.) either dissolved in an aqueous buffer solution or suspended in sesame oil was studied. Both subcutaneous injection and oral administration of the drugs were used. It was observed that the injections of oil suspensions of sodium penicillin were as effective as the injections of buffered aqueous solutions of this drug.

By subcutaneous injection, the pure benzyl penicillin appeared to be at least three times as potent as pure sodium penicillin on a weight basis. If an allowance is made for the difference in molecular weights, the ratio becomes even greater. The pure benzyl ester was found to be 7.5 times as effective as an equimolecular quantity of commercial sodium penicillin.

Administration of a crude benzyl penicillin (50 per cent pure) by mouth revealed that, in mice, about ten times more was required than when it was given subcutaneously. Mice appeared to absorb water-soluble penicillin more efficiently, however, since only three times as much of either pure or commercial sodium penicillin was required by mouth as by subcutaneous injection.

Clinical data on patients are to be published elsewhere.

Extrathyroid Effects of Thiouracil Therapy. E. H. Fishberg and J. Vorzimer. *J. A. M. A. 128,* 915 (1945). Observations made on 96 patients treated with thiouracil for hyperthyroidism indicated that this drug brings about a reduction of the basal metabolic rate and exerts a favorable effect on extrathyroid complications caused

by the heightened basal metabolism or by a disturbance of glandular equilibrium, or both.

Its usefulness is, however, limited by its toxicity. In 20 per cent of the cases treated a sudden granulopenia was noted. The authors emphasize the necessity for performing a white blood count every second or third day, discontinuing the drug immediately if there is a sudden drop in the total leukocyte count, or if the granulocytes decrease to less than 45 per cent. An abrupt rise in temperature, accompanied by arthralgia, myalgia, lymphadenopathy or the appearance of a rash, also indicates discontinuance of thiouracil therapy.

The usual dosage was 1 gm. daily for three days, followed by 0.6 gm. until the basal metabolic rate dropped to approximately + 10 or less. The maintenance dose required thereafter varied, some patients requiring more than 0.2 gm. daily; in 15 cases of sustained remission for a number of months, all medication was discontinued.

Fourteen case reports are presented.

Rectal Instillation of Aminophylline in Intractable Asthma. A. L. Barach. *J. A. M. A. 128,* 589 (1945). The author describes the technic of administering aminophylline by rectal instillation for the relief of bronchial spasm in asthma.

The apparatus consists of a 20 cc. glass syringe, to which is attached one end of a rubber tube (⅛ inch diameter x 18 inches in length); by means of a short glass tube, the other end is joined to a No. 12 French rubber catheter.

The recommended dosage is either 0.48 gm. (the amount contained in a 20 cc. ampul for intravenous use), or about 0.6 gm. of the drug dissolved in tap water at the time of administration.

From ten to thirty minutes are required for the relief of bronchial spasm; while this is not as prompt as by intravenous technic, it has the advantage of but rarely causing the side effects of dizziness and faintness. By using the method described, the patient may readily administer the drug to himself.

It has been observed that some patients become refractory to aminophylline. In such cases the drug must be discontinued and other methods of bronchial relaxation substituted, such as helium-oxygen therapy or colonic ether, in order to restore the patient's responsiveness to aminophylline.

Toxicity and Potential Dangers of Aerosols and Residues From Such Aerosols Containing Three Per Cent DDT (Second Report). P. A. Neal, W. F. von Oettingen, R. C. Dunn and N. E. Sharpless. *Supplement No. 183, Public Health Rep.* An aerosol consisting of three per cent DDT in a primary solvent (5 per cent), a secondary oil solvent (5 per cent), and pyrethrin (0.4 per cent) in a propellant base, was dispersed into a sealed, non-ventilated glass chamber having a capacity of 409.7 liters in such amounts as to produce an initial concentration of 26.4 to 32.9 mg. of DDT per liter of air. Under such conditions, a single exposure for 45 minutes was fatal to over 50 per cent of immature mice, and to about 15 per cent of adult mice and immature rats, but not to adult rats or adult guinea pigs.

The effects of repeated exposure to high concentrations of the aerosol in air were studied in four series of experiments. In the first series, a concentration of 0.11 mg. of DDT per liter of air, which is about twenty times the amount required as an insecticide, was tested on adult mice and adult rats for 50-minute periods three times daily, five days per week, for eight weeks. Such exposure was definitely toxic to mice, but not to rats.

Observations were made on dogs in the second series. The amount of aerosol dispersed into the glass chamber corresponded to a mean initial concentration of 33 mg. of DDT per liter, and the animals were exposed once daily for 45 minutes, five days per week, for eight weeks. By means of control observations it was demonstrated that any toxic effects noted in the dogs so treated were caused by the primary solvent, not by DDT.

In the third series, exposure of *Rhesus* monkeys according to the procedure used for the dogs, but for a period of 22 weeks, failed to cause either definite nervous symptoms characteristic of DDT toxicity or liver injury.

In the fourth series, dogs were exposed to massive concentrations of DDT, but it was demonstrated on control animals that the toxic symptoms observed were caused by constituents of the aerosol other than DDT.

The percutaneous absorption of DDT was studied on mice and dogs by applying a residue of the aerosol (containing no propellant) to the skin between the shoulder blades, the fur having been removed from the area by clipping. A single application of 0.1 cc. of the resi-

due caused death in the majority of the mice, and smaller doses caused toxic effects definitely attributable to DDT. The dogs received daily applications of 1 cc. per Kg. of body weight, five days per week, for about three weeks. Classical DDT poisoning was not observed in these animals, but three out of four of them died with signs of severe depression.

Studies of the irritant action of the DDT aerosol residue on the eye were performed on rabbits. It was shown that the lachrymation, inflammation and other symptoms noted were not caused by DDT, but presumably by the primary solvent and pyrethrin.

The subcutaneous injection of 1 cc. per Kg. of the aerosol residue (corresponding to 200 mg. of DDT) caused only slight local irritation in rabbits, and it was demonstrated that this was produced by constituents other than DDT.

In contrast, the intraperitoneal injection of the same dose caused moderate irritation of the peritoneal cavity in the rabbit, possibly due to the deposition of the insoluble DDT on the peritoneal lining.

SOLID EXTRACTS

Russia has 130,000 physicians today as compared with 20,000 in 1913. The government is expanding its medical education to increase this number considerably. Medical students are accepted with ability as the primary requirement and almost all receive government subsidies so that they can devote themselves exclusively to their studies.

AJP

The experimental use of DDT as a means of controlling poliomyelitis in certain areas is based upon the following established facts according to Dr. Gudakunst, Director of the National Foundation.

(1) Flies have been shown to carry poliomyelitis virus; (2) experimental animals have been infected from these flies; (3) food contaminated by flies in an epidemic area likewise produced poliomyelitis in the experimental animal.

It is not known if flies play an important role or any role in the spread of this disease in humans. The study with DDT may give some information on this point.

AJP

The growth of the American drug industry has been truly remarkable. During the war the world relied on us for many of its drugs. In 1944 foreign sales of drugs amounted to $106,000,000. The production of certain drugs was stupendous. Thus in 1944 we produced 10,000,000 pounds of sulfonamides, 160,000,000,000 units of penicillin and 1300 tons of vitamins.

AJP

Hay fever in the broad sense causes suffering to over 6,500,000 people in the United States. Although desensitization treatments help many individuals, it is indeed a biochemical mystery why some people show allergy to pollen and others do not. Some day when cell physiology is better understood, allergy, cancer and other conditions may be conquered.

A new group of sulfonamides have been developed which seem superior to the customary ones according to preliminary tests. The most active of this group, known as sulfanilyl 3,5-dibromoanilide, is effective against certain sulfonamide resistant organisms and is not inhibited in its action by paraaminobenzoic acid.

AJP

Almost unbelievable properties are reported for some new products described as "silicones." These are large molecules made up of silicon and oxygen and among them is a liquid which flows like water at 70 degrees below zero, a grease that doesn't melt at 400 degrees, and a rubber that withstands almost any extreme of temperature. Using it as insulation, motors can run hot without burning out and can even produce higher horsepower.

AJP

A profilometer which measures surface roughness to within a millionth of an inch is described in a recent publication by Westinghouse. So delicate is it that a dust-free environment must be maintained in the room in which it is housed and the air maintained at constant temperature and humidity.

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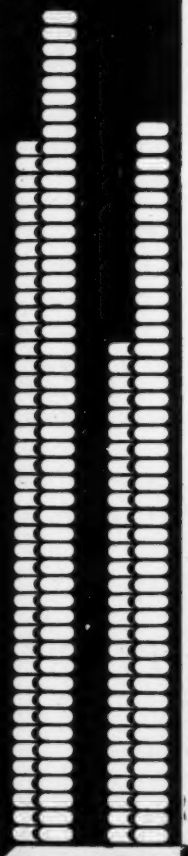

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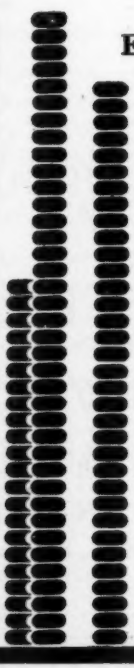

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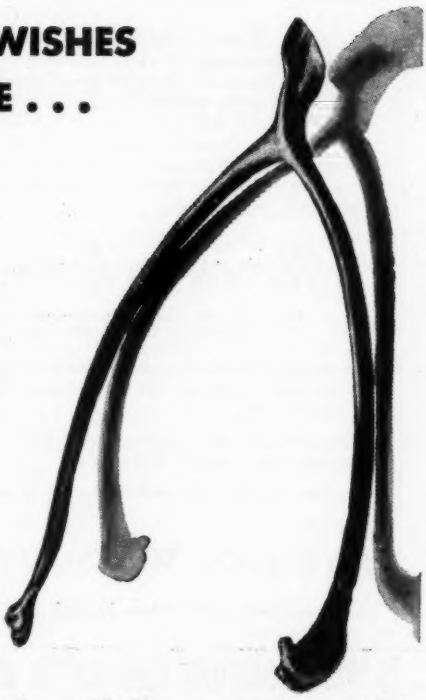

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